

7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring malathion, its metabolites, and other biomarkers of exposure and effect to malathion. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

7.1 BIOLOGICAL SAMPLES

In mammals, malathion is metabolized by hydrolytic cleavage of one or both succinate esters and by hydrolysis of the succinate moiety from the dialkylthiophosphate (see Section 3.4.3, Metabolism). The primary metabolites found in biological fluids following exposure to malathion are malathion dicarboxylic acid (DCA) and malathion monocarboxylic acid (MCA). The DCA and MCA carboxylic acids represent more than 80% of the total metabolites excreted in urine. In addition, smaller amounts of two other metabolites, *O,O*-dimethyl phosphorothionate (DMTP) and *O,O*-dimethyl phosphorodithioate (DMDTP) are also found. Metabolites may also arise from malaoxon, metabolite of malathion.

The principal method used for the detection of malathion and metabolites in biological samples is gas chromatography (GC) using an electron capture detector (ECD), a nitrogen/phosphorous detector (NPD), a flame photometric detector (FPD) in phosphorous mode, or a mass spectroscopy detector (MS). The detection of malathion using GC-FID is reported to have low sensitivity and results are generally not reproducible (Lin and Hee 1998). Confirmation of GC analysis is typically accomplished using gas chromatography with mass spectroscopy (GC-MS). The preparation of samples for GC analysis typically involves sample extraction with an organic solvent (e.g., hexane or diethyl ether) and purification of the extract (e.g., by column chromatography or further extraction). The major metabolites of malathion, DCA and MCA, require derivatization prior to GC analysis.

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Exposure to organophosphorous pesticides is generally assessed by monitoring: blood cholinesterase (ChE) inhibition and urinary metabolite excretion. Assay of blood cholinesterase activities is the most common and reliable biological indicator of human exposure to organophosphorous pesticides (OPs). The OPs inhibit acetylcholinesterase (AChE) in red blood cells (RBCs) and pseudocholinesterase (PChE) in serum or plasma. Depending upon the degree of exposure, type of OPs, and AChE/PChE, the reduction in PChE and AChE activity can last for several days. Malathion and its activated product, malaxon, are not good inhibitors of cholinesterases. Several analytical methods have been developed to determine AChE and PChE in blood. Results obtained from the methods are generally comparable, but differ widely in accuracy, sensitivity, and precision. Analytical methods for detection of metabolites of malathion in urine are more sensitive than those used to determine AChE and PChE in blood. Because of the increase in sensitivity, the methods are capable of revealing exposures that may be insufficient to bring about a toxic response. However, since alkyl phosphates such as malathion are rapidly metabolized in the body and their metabolites are excreted in urine within a short time (24–36 hours), urine samples for analysis must be collected quickly. Table 7-1 summarizes the analytical methods used to detect malathion and its metabolites as well as cholinesterase activity in biological tissues and fluids.

Malathion has been determined in human serum using a hexane extraction procedure and detection using GC-FPD (Fournier and Sonnier 1978). It was necessary to perform serum assays within 48 hours of patient exposure since malathion is quickly hydrolyzed in human tissues. The limit of detection was reported as 0.2 mg/L.

The quantity of malathion, DCA, and MCA in rat and human urine has been measured using GC-FPD (Bradway and Shafik 1977). Sample preparation required an extensive clean-up procedure involving extraction with diethyl ether, centrifugation, acidification, and additional extractions. The extracted DCA and MCA was then derivatized by ethylation or methylation and purified by column chromatography on silica gel using an ethyl acetate/benzene eluent. The percent recoveries for MCA and DCA from samples of rat urine were 99–104% for MCA and 98–101% for DCA. The lowest limit of detection in rat and human urine was 0.005 mg/L for MCA and 0.002 mg/L for DCA; the detection limits were found to be dependent upon detector sensitivity and the presence of interfering peaks in the GC. This procedure is commonly used, but difficulties have been reported with extraction and derivativization (Ito et al. 1979). Significant background interference in GC analysis can occur when inorganic phosphates are present (Moody et al. 1985). Derivatives of DMTP and DMDTP have been measured in human urine using GC-FPD in phosphorous mode (Fenske and Leffingwell 1989). Urine samples were

Table 7-1. Analytical Methods for Determining Malathion or Biomarkers of Exposure in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Human blood	Collection of blood samples, 0.1 M phosphate buffer (pH=8.0)	Spectrophotometer (at 410–412 nm)	No data	No data	Ellman et al. 1961
Human blood	Collection of blood samples, tris(hydroxymethyl)aminomethane, sodium chloride, HCl, centrifuge	Colorimeter analysis (at 412 nm)	No data	No data	Knaak et al. 1978
Blood	Microtiter assay using acetylthiocholine, AChE, Ellman assay reaction mixture	Microtiter assay; absorbance measurement (at 405 nm)	No data	No data	Doctor et al. 1987
Human serum	Extraction with hexane	GC-FPD	0.001 mg/L	No data	Fournier and Sonnier 1978
Human urine	Extract with diethyl ether, centrifuge, acidify, extract with hexane, alkylate with BF ₃ -methanol, purify on silica gel (elution with benzene/ethyl acetate)	GC-FPD	0.002 mg/L (DCA) 0.005 mg/L (MCA)	98–101% for DCA 98–104% for MCA	Bradway and Shafik 1977
Human urine	Hydrolysis of MCA and DCA with 1.0 N KOH, 90 EC, 4 hours, extraction with hexane, derivatization with PFBB	GC-FPD (phosphorous mode)	0.014 mg/L (DMTP) 0.025 mg/L (DMDTP)	88% (total malathion) 120% (DMTP) 70% (DMDTP)	Fenske and Leffingwell 1989

**Table 7-1. Analytical Methods for Determining Malathion or Biomarkers of Exposure in Biological Samples
(continued)**

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Human urine	Solid-phase extraction, methanolic HCl extraction, derivatization with diazomethane,	Isotope dilution Ion Trap GC-MS	6.5 ng/mL (DCA) 4.4 ng/mL (MCA)	106–114% (DCA) 50–60% (MCA)	Draper et al. 1991
Human urine	Acidify to pH 3.7, extract twice with CH ₂ Cl ₂ /diethyl ether (1:4), centrifuge and concentrate	Isotope dilution HPLC/MS/MS	0.5 µg/L (DCA)	75%	Baker et al. 2000; Beeson et al. 1999

DCA = malathion dicarboxylic acid; DMDTP = O,O-dimethyl phosphorodithionate; DMTP = O,O-dimethyl phosphorothionate; FPD = flame photometric detection; GC = gas chromatography; HCl = hydrochloric acid; HPLC = high performance liquid chromatography; KOH = potassium hydroxide; M = Molar; MCA = malathion monocarboxylic acid; MS = mass spectrometry; PFBB = pentafluorobenzyl bromide

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subjected to alkaline hydrolysis to convert DCA and MCA to DMTP and DMDTP, which were derivatized with pentafluorobenzyl bromide. However, the procedure is not specific for malathion since DMTP and DMDTP are common to several types of organophosphorous insecticides. The detection limit was 0.014 mg/L for DMTP and 0.025 mg/L for DMDTP. Ion-exchange resins and anion-exchange solid-phase extraction have been used to isolate metabolites of malathion from urine (Lores and Bradway 1977; Muan and Skare 1989). The MCA, DCA, DMDTP, and DMTP metabolites were derivatized with diazomethane and assayed using GC-NPD. A detection limit of 2 µg/mL for each metabolite was reported. A later modification of this procedure utilized isotope dilution ion trap GC-MS to detect the diazomethane derivatives to improve the detection limits. The lowest limits of detection for DCA and MCA were 0.006 and 0.004 mg/L, respectively.

A recent method for identifying and quantifying malathion diacid in urine samples collected from nonoccupationally exposed populations utilizes isotope dilution high-performance liquid chromatography/tandem mass spectrometry (HPLC/MS/MS); the method has the advantage of not requiring derivatization of DCA (Baker et al. 2000; Beeson et al. 1999). Using this method, urine samples are acidified (10% sulfuric acid) to a pH of 3.7 and extracted with methylene chloride and ethyl ether (1:4). The organic extracts are combined and concentrated for HPLC injection and MS/MS analysis. The analytical limit of detection was 0.0005 mg/L and the recovery was 75%. The advantages of this technique are the high specificity and sensitivity that are achieved by chromatographically separating out unwanted contaminants that could interfere with the mass analysis and the use of isotope dilution to correct for sample recoveries.

The most commonly used assay for determining ChE activity is that of Ellman et al. (1961). In this method, RBCs are suspended in a buffer (e.g., 10 µL blood in 6 mL of 0.1 M phosphate buffer). For assay of only RBC ChE, the suspension is treated with quinidine sulfate to inhibit PChE. Total esterase activity is determined in the samples with no addition of quinidine sulfate. The production of thiocholine formed in the hydrolysis of acetylthiocholine is measured by coupling of the reactive thiol with 5,5'-dithio-bis(2-nitrobenzoate) (DTNB) to give a thionitrobenzoate (TNB). The TNB is a yellow anion and its formation can be measured spectrophotometrically. The production of TNB is rapid and the concentration of DTNB used in the assay does not inhibit the enzyme. Absorbance is typically measured at 410–412 nm, but other wavelengths have been used. Because a nonlinear reaction of the thiol reagent with reduced glutathione of RBCs is possible, a sample blank is required. This method has been adapted to assay cholinesterase in other tissues such as lung, brain, liver, stomach, heart, and muscle. An

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adaptation of the Ellman assay is a microtiter assay method for AChE that has been developed by Doctor et al. (1987). The AChE samples to be assayed are added to microtiter plates and enzymatic hydrolysis is initiated by adding Ellman reaction mixture (DTNB). The hydrolysis reaction is terminated by the addition of an AChE inhibitor (1,5-bis(4-allyldimethylammoniumphenyl)-pentan-3-one dibromide). The absorbance of the microtiter can be measured continuously by reader at 405 nm filter.

Several modified versions of the Ellman assay have been developed, including an automated procedure that is used by the State of California to monitor exposure of field workers (Knaack et al. 1978). In this method, samples of whole blood and plasma are diluted with tris(hydroxymethyl)aminomethane (0.05 Molar) and sodium chloride (0.114 Molar) buffer adjusted to pH 7.7 with hydrogen chloride. The samples are centrifuged at 1,600 rpm for 4 minutes to separate RBCs from plasma, which are then analyzed for esterase activity using a continuous flow Technicon Analyzer. Prediluted whole blood or plasma samples are passed through a 37 EC dry bath incubator for 1.17 minutes. The sample is then passed through a 12 inch dialyzer equipped with a Type C membrane and the released thiocholine is passed through a solution of DTNB color reagent. The thiocholine DTNB mixture is sent to a delay coil for color development prior to being passed through a 15x1.5 mm flow cell.

7.2 ENVIRONMENTAL SAMPLES

The principal method that is used to analyze environmental samples for malathion is GC. Detectors that are used include FPD in phosphorous mode, ECD, and MS. Another method that has also been used successfully is GC with tandem ion trap MS/MS. Table 7-2 summarizes the analytical methods used to detect malathion and its metabolites in environmental samples.

Malathion has been detected in air using GC equipped with FPD and a nitrogen-phosphorous detector and with GC-MS. The lowest limit of detection reported was in the 0.5–1.0 ng/m³ range. Several methods of sample collection have been reported and include collection on resin and filter paper (Brown et al. 1993b), a combined filter-sorbent tube sampler (OSHA Versatile sampler; Kennedy et al. 1994), a glass wool-Tenax TA tube (Roinestad et al. 1993), a polyethylene-backed adsorbent paper (Brown et al. 1991), and air samplers equipped with Ortho 42 tubes (Wright et al. 1996). Sample preparation typically involves desorption of analytes from the tubes using organic solvent (e.g., acetone, acetone-toluene, and acetone-hexane-toluene) (Brown et al. 1993b). Recoveries were reported to be in the 90-100% range. The 100% recovery of malathion was reported by Kennedy (1994) during a study of indoor household

Table 7-2. Analytical Methods for Determining Malathion in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (indoor)	Adsorption onto sample tube containing 25 mg TENAX TA and desorption with acetone	GC-MS with chemical ionization	1.0 ng/m ³	100%	Roinestad et al. 1993
Air	Collection on glass cartridges containing XAD-2 resin, extract with acetone	GC-FPD (in phosphorous mode)	No data	No data	Brown et al. 1993
Air	Adsorption on OVS, desorption with acetone-toluene (1:9)	GC-FPD (in phosphorous mode)	0.05 µg/mL	94%	Kennedy et al. 1994
Air (indoor)	Brian Model Air Sampler (Ortho 42 tubes), extract with toluene:hexane:acetone (1.0:0.5:0.5)	GC with NPD and GC-FPD (in phosphorous mode)	No data	90%	Wright et al. 1996
Water	Extracted with hexane	GC-FPD	0.06 µg/L	117%	Zweig and Devine 1969
Water	Adsorption onto a macroreticular resin (Amberlite XAD-2), desorb with acetone-hexane (15:85)	GC-NPD (or GC-FID)	20 pg (0.02 ng/L)	96–103%	Label et al. 1979
Water	Absorption into a microfiber (SPME), desorb directly in GC injector	GC-NPD	0.04 ng/mL (40 ng/L)	No data	Beltran et al. 1998
Water	Adsorption onto a macroreticular resin (Amberlite XAD-2), desorption with diethyl ether, concentrate, hydrolyze to DMDTP, complex with Bi(III), and extract with CCl ₄	Colorimetric	0.023 mg/L	95%	Clark and Qazi 1980
Water	SFE-CO ₂ +0.3 mL methanol, 50 EC, 350 bar	GC-MS	No data	85%	Barnabas 1994
Water	SPE elution with methylene chloride-methanol (80:20)	GC-MS (ion trap)	0.12 µg/L	51%	Eitzer and Chevalier 1999
Soil	Soxhlet extraction with acetone-hexane	GC-ECD	No data	79%	Kramer et al. 1999

Soil	Microwave assisted extraction with acetone-hexane	GC-ECD	No data	75%	Kramer et al. 1999
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Table 7-2. Analytical Methods for Determining Malathion in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Soil	Subcritical water extraction with deionized water	GC-ECD	No data	9%	Kramer et al. 1999
House dust	Soxhlet extraction with 6% diethyl ether in <i>n</i> -hexane	GC-ECD; GC-MS	50–1,500 ng/g	75%	Lewis et al. 1994
House dust	Soxhlet extraction with 6% diethyl ether in <i>n</i> -hexane	GC-FPD (or NPD) and GC-MS	50 ppb	92%	Bradman et al. 1997
Handwipe (children)	Wiping hands with sterile gauze with propanol, extract with diethyl ether in <i>n</i> -hexane	GC-FPD	50 ppb	92%	Bradman et al. 1997
Soil	SFE-CO ₂ +5% methanol, 50 EC, 250 bar, 15 minute static, 30 minute dynamic	GC-MS	No data	76.3–96.7%	Camel 1997
Food (grains)	SFE-CO ₂ , 40 EC, 450 bar, dynamic	GC-FPD	No data	Greater than 80%	Camel 1997
Food (fruits, vegetables, and milk)	Extract with acetonitrile-ethanol (95:5, v/v), SPE (Envi-Carb) using acetonitrile-toluene (3:1, v/v)	GC with tandem ion trap MS/MS	ppb	No data	Sheridan and Meola 1999
Fruit	Extract the flower or fruit with acetone, partition with water/hexane, column chromatography on Florisil using 20% acetone in hexane (v/v)	GC/ECD	0.0005 ppm (0.05 ppb)	Greater than 95%	Belanger et al. 1990
Potato	SFE-CO ₂ , 60 EC, 320 bar, 2 minute static, 10 minute dynamic	GC-MS	No data	72–94%	Camel 1997
Vegetable, fruit	Extraction with ethyl acetate	GC-FPD (phosphorous mode) and GC-MS	5–20 µg/kg	105%	Aguera 1993

Table 7-2. Analytical Methods for Determining Malathion in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Edible fat	SFE (CO ₂ -3% acetonitrile; 60 EC; 27.58 Mpa) column chromatography on florisil	GC-FPD (phosphorous mode)	No data	80–85%	Hopper 1999
Milk (whole, skim, infant formula)	Extraction with acetone-acetonitrile, centrifuge, partition with dichloromethane/water, solid phase extraction with acetonitrile, chromatography on a C18 (SPE) cartridge	GC-FPD (phosphorous mode)	No data	86–103%	Erney 1995

DMDTP = O,O-dimethyl phosphorodithionate; ECD = electron capture detector; FID = flame ionization detector; FPD = flame photometric detection; GC = gas chromatography; LC = liquid chromatography; MS = mass spectrometry; NaCl = sodium chloride; NPD = nitrogen/phosphorus detector; OSHA = Occupational Safety and Health Administration; OVS = OSHA versatile sample; SFE = supercritical fluid extraction; SFE-CO₂ = supercritical fluid extraction with carbon dioxide; SPE = solid phase extraction; SPME = solid-phase micro extraction; ppb = parts per billion; ppm = parts per million; v/v = volume/volume

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air. Sample preparation was accomplished by desorption of malathion from a collection tube using acetone. The solution was concentrated and analyzed using GC-MS with chemical ionization (Kennedy et al. 1994). The limit of detection was reported as 0.5 ng/m³.

In water, malathion can be analyzed using colorimetric analysis, GC-FPD, GC-NPD, and GC-MS. The isolation of malathion from water generally requires sample extraction followed by purification of the extract to remove substances that may interfere with detection methods. Several methods have been developed for the extraction of malathion from water samples involving extraction with an organic solvent (Zweig and Devine 1969); collection on a resin column followed by elution with an organic solvent (Clark and Qazi 1979; LeBel et al. 1979); and solid-phase extraction and elution with an organic solvent (Eitzer and Chevalier 1999). Recent work by Beltran et al. (1998) has demonstrated that solid-phase micro extraction (SPME) can be used to identify organophosphorous pesticides in water samples without the use of organic solvents. Organophosphorous compounds can be extracted from water onto a polymeric (polydimethylsiloxane or polyacrylate) collection filter according to their affinity for the filter coating and are subsequently thermally desorbed from the coating directly in the GC injector. The limit of detection for malathion was 0.04 ng/mL (Beltran, et al. 1998). In another study, the mean percent recovery of malathion from water using SPME was found to be very low, suggesting that the technique may require further investigation to optimize partitioning of pesticides to the collection fiber (Kramer et al. 1999). Supercritical fluid extraction (SFE), a process using carbon dioxide liquified above 31 EC at high pressure, provides efficient extraction of pesticides and their metabolites in a variety of matrices without the use of large quantities of organic solvents (Camel 1997). A modified SFE using methanol-CO₂, was used to obtain recoveries of 84.6% for malathion from water (Barnabas et al. 1994).

Analytical analysis of soils, sand, sediments, and indoor house dust has been performed using GC-ECD, GC-FPD, GC-NPD, and GC-MS; analysis of food, milk (whole, and infant formula), and edible fat has been accomplished using GC-FPD, GC-ECD, GC-MS, and tandem GC-MS/MS. Sample preparation methods vary widely since extraction and cleanup methods are dependent upon the sample matrix. For soils and sediments, soxhlet extraction is the standard extraction technique used in most EPA methods (Smith 1994). Pesticide residues in house dust have been determined using soxhlet extraction (6% diethyl ether in hexane). Recoveries of malathion were reported to be 75–92% with a limit of detection of 0.05–1.5 mg/ng (Bradman et al. 1997; Lewis et al. 1994). In a recent study of organophosphorous pesticides, Kramer et al. (1999) examined various extraction techniques and compared their percent recoveries. For malathion, soxhlet extraction was found to have slightly higher recoveries (79%; average

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of three extractions) than microwave assisted extraction (75%; average of five extractions). Standard procedures for the extraction of milk and fat involve the complete extraction of the fat, extensive cleanup by column chromatography on Florisil prior to analysis (AOAC 1990; PAM 1994). To simplify these procedures, Erney (1995) developed a method that utilizes solid-phase extraction for the cleanup. Using this method, recoveries of 86–103% were obtained for malathion in whole and skim milk, and in infant formula (Erney 1995). In a recent study, SFE was used successfully to extract organophosphorous pesticides from edible fats. Although the method was determined to be less effective than standard procedures for the recovery of some analytes, the recovery of malathion was 80–85% (Hopper 1999). The use of GC with ion trap mass spectrometry (MS/MS) has been investigated by Sheridan and Meola (1999) for analysis of food matrixes. Because MS/MS is highly selective, it is capable of making clear compound identification of even complex matrixes at the parts-per-billion range and is less susceptible to interfering coextractives than selective detectors (e.g., ECD and FPD). Using GC-MS/MS, malathion was detected in strawberries at 0.01 ppm. In contrast, detection of malathion using a selective detector was 0.009 ppm (Sheridan and Meola 1999).

Analysis of handwipe samples taken from children has been accomplished using GC-FPD or GC-NPD. Detection limits were reported as 50 ppb ($\mu\text{g/L}$) with an average recovery of 92% (Bradman et al. 1997).

7.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of malathion is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of malathion

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

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7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Organophosphate pesticides, such as malathion, inhibit cholinesterases. Methods exist for the measurement of erythrocyte and plasma cholinesterase levels (EPA 1980d; Nabb and Whitfield 1967). However, there are some problems with the reliability of these methods because normal erythrocyte cholinesterase values vary widely (Midtling et al. 1985; Tafuri and Roberts 1987) and plasma cholinesterase can be suppressed by a variety of diseases (Henry 1984; Tafuri and Roberts 1987). Further studies to improve the reliability of cholinesterase levels might be useful in establishing this as a reliable measure of organophosphate exposure.

Methods for Determining Parent Compounds and Degradation Products in Environmental

Media. Analytical methods exist to measure low levels of malathion in air (Brown et al. 1993b; Kennedy et al. 1994; Roinestad et al. 1993; Wright et al. 1996); water (Beltran et al. 1998; Clark and Qazi 1979; Eitzer and Chevalier 1999; LeBel et al. 1979; Zweig and Devine 1969); soil; carpet dust; milk; infant formula; fats and oils; and foods (Bradman et al. 1997; Erney 1995; Hopper 1999; Kramer et al. 1999; Lewis et al. 1994; Sheridan and Meola 1999). These methods can be used to identify potentially contaminated media and that may be a source of human exposure. Several analytical methods exist for the detection of malathion. Gas chromatography coupled with sensitive phosphorous detectors and GC-MS are the most commonly used methods of detection. The detection limit is typically in the low parts-per-billion for air (Kennedy et al. 1994), water (Eitzer and Chevalier 1999), and soil; carpet dust; milk; infant formula; and foods (Bradman et al. 1997; Lewis et al. 1994; Sheridan and Meola 1999). Studies are needed to investigate improved methods of isolation from complex matrixes, selectivity of detection, precision, and accuracy.

7.3.2 Ongoing Studies

No information was located concerning ongoing studies for improving methods of analysis of malathion metabolites, or other biomarkers of exposure and effect for malathion in biological materials.